Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 2 of 14

## II. Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

- 1. (Canceled)
- 2. (Currently Amended) A compound of formula (I) or a pharmaceutically acceptable salt thereof, wherein the compound of formula (I) is:

$$R_1$$
 $R_2$ 
 $R_3$ 
 $R_4$ 
 $R_5$ 
 $R_6$ 
 $R_7$ 
 $R_7$ 

wherein the dotted lines indicate a single or a double bond;

 $R_1$  is  $-OD_1$  or -Cl;

 $R_2$  and  $R_8$  are a hydrogen; or  $R_1$  and  $R_2$  taken together are  $=CH_2$  or =O;

R<sub>3</sub> and R<sub>4</sub> are each independently a hydrogen, -OD<sub>1</sub> or -CH<sub>3</sub>;

R<sub>5</sub> and R<sub>6</sub> are each independently a hydrogen, -OD<sub>1</sub>, -CH<sub>3</sub>, -OCH<sub>3</sub> or -CH=CH<sub>2</sub>;

 $R_7$  is a hydrogen or  $-OD_1$ ;

 $R_9$  is hydrogen or absent when the carbon to which it is attached is the central carbon of an allene functionality; or  $R_8$  and  $R_9$  taken together with the chain to which they are attached form a substituted benzene ring with the proviso that  $R_1$  is an oxygen atom which is attached to the carbon atom at the position of the benzene ring defined by B;

A is 
$$-CH=$$
,  $-CH_2$ ,  $-S-$ , or  $-O-$ ;

X is  $-CH_2OR_{11}$ ,  $-C(O)OR_{11}$  or  $-C(O)N(D_1)R_{12}$ ;

 $R_{11}$  is  $D_1$ , a lower alkyl group, or

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 3 of 14

 $R_{12}$  is  $-S(O)_2CH_3$  or  $-C(O)CH_3$ ;

Z is (a) an ethyl, (b) a butyl, (c) a hexyl, (d) a benzyl,

R<sub>13</sub> is a hydrogen or –Cl;

 $D_1$  is a hydrogen or D; with the proviso that at least one  $D_1$  in formula (I) must be D;

D is Q or K;

Q is -NO or -NO<sub>2</sub>;

K is  $-W_a-E_b-(C(R_e)(R_f))_p-E_c-(C(R_e)(R_f))_x-W_d-(C(R_e)(R_f))_y-W_i-E_j-W_g-(C(R_e)(R_f))_z-T-Q;$  with the proviso that when X is  $-C(O)OD_1$  and  $D_1$  is K, then K is not an alkyl, branched alkyl or cycloalkyl mononitrate; a benzoic acid substituted benzyloxy mononitrate; the regioisomeric esters of glycerol dinitrate and oligomers thereof;

a, b, c, d, g, i and j are each independently an integer from 0 to 3;

p, x, y and z are each independently an integer from 0 to 10;

W at each occurrence is independently -C(O)-, -C(S)-, -T-, -(C(R<sub>e</sub>)(R<sub>f</sub>))<sub>h</sub>-, an alkyl group, an aryl group, a heterocyclic ring, an arylheterocyclic ring, or -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>-;

E at each occurrence is independently -T-, an alkyl group, an aryl group, - $(C(R_e)(R_f))_h$ -, a heterocyclic ring, an arylheterocyclic ring, or - $(CH_2CH_2O)_q$ -;

h is an integer form 1 to 10;

q is an integer from 1 to 5;

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 4 of 14

 $R_e$  and  $R_f$  are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialylamino, an arylamino, an alkylamino, an alkylamino, an alkylamino, an alkylamino, an alkylamino, an arylalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cycloalkylthio, a cycloalkenyl, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, a carbamate, an alkylcarboxylic acid, an arylcarboxylic acid, an arylcarboxylic ester, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, a sulfonic ester, a urea, a phosphoryl, a nitro, -T-Q, or  $(C(R_e)(R_f))_k$ -T-Q, or  $R_e$  and  $R_f$  taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group or a bridged cycloalkyl group;

k is an integer from 1 to 3;

T at each occurrence is independently a covalent bond, a carbonyl, an oxygen,  $-S(O)_o\text{- or -}N(R_a)R_i\text{-};$ 

o is an integer from 0 to 2;

Ra is a lone pair of electrons, a hydrogen or an alkyl group;

 $R_i$  is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an arylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylaryl, an alkylsulfinyl, an alkylsulfinyl, an arylsulfinyl, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an amino alkyl, an amino aryl,  $-CH_2-C(T-Q)(R_e)(R_f)$ , or  $-(N_2O_2-)^{\bullet}M^+$ , wherein  $M^+$  is an organic or inorganic cation; with the proviso that when  $R_i$  is  $-CH_2-C(T-Q)(R_e)(R_f)$  or  $-(N_2O_2)^{\bullet}M^+$ , or  $R_e$  or  $R_f$  are T-Q or  $(C(R_e)(R_f))_k-T-Q$ , then the "-T-Q" subgroup can be a hydrogen, an alkyl, an alkoxy, an alkoxyalkyl, an aminoalkyl, a hydroxy, a heterocyclic ring or an aryl group;

with the proviso that the compound of formula (I) has at least one NO<sub>2</sub> group linked through an oxygen atom, a nitrogen atom or a sulfur atom.

3. (Currently Amended) The compound of claim 2, wherein the compound of formula (I) comprising at least one NO group, at least one NO<sub>2</sub> group, or at least one NO and

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 5 of 14

NO2-group is a nitrosated arbaprostil, a nitrosylated arbaprostil, a nitrosated and nitrosylated arbaprostil, a nitrosated alprostadil, a nitrosylated alprostadil, a nitrosated and nitrosylated alprostadil, a nitrosated beraprost, a nitrosylated beraprost, a nitrosated and nitrosylated beraprost, a nitrosated carboprost, a nitrosylated carboprost, a nitrosated and nitrosylated carboprost, a nitrosated cloprostenol, a nitrosylated cloprostenol, a nitrosated and nitrosylated cloprostenol, a nitrosated dimoxaprost, a nitrosylated dimoxaprost, a nitrosated and nitrosylated dimoxaprost, a nitrosated enprostil, a nitrosylated enprostil, a nitrosated and nitrosylated enprostil, a nitrosated enisoprost, a nitrosylated enisoprost, a nitrosated and nitrosylated enisoprost, a nitrosated fluprostenol, a nitrosylated fluprostenol, a nitrosated and nitrosylated fluprostenol, a nitrosated fenprostalene, a nitrosylated fenprostalene, a nitrosated and nitrosylated fenprostalene, a nitrosated gemeprost, a nitrosylated gemeprost, a nitrosated and nitrosylated gemeprost, a nitrosated latanaprost, a nitrosylated latanaprost, a nitrosated and nitrosylated latanaprost, a nitrosated limaprost, a nitrosylated limaprost, a nitrosated and nitrosylated limaprost, a nitrosated meteneprost, a nitrosylated meteneprost, a nitrosated and nitrosylated meteneprost, a nitrosated mexiprostil, a nitrosylated mexiprostil, a nitrosated and nitrosylated mexiprostil, a nitrosated misoprostol, a nitrosylated misoprostol, a nitrosated and nitrosylated misoprostol, a nitrosated misoprost, a nitrosylated misoprost, a nitrosated and nitrosylated misoprost, a nitrosated misoprostol acid, a nitrosylated misoprostol acid, a nitrosated and nitrosylated misoprostol acid, a nitrosated nocloprost, a nitrosylated nocloprost, a nitrosated and nitrosylated nocloprost, a nitrosated ornoprostil, a nitrosylated ornoprostil, a nitrosated and nitrosylated ornoprostil, a nitrosated prostalene, a nitrosylated prostalene, a nitrosated and nitrosylated prostalene, a nitrosated PGE1, a nitrosylated PGE1, a nitrosated and nitrosylated PGE<sub>1</sub>, a nitrosated PGE<sub>2</sub>, a nitrosylated PGE<sub>2</sub>, a nitrosated and nitrosylated PGE<sub>2</sub>, a nitrosated  $PGF_1$ , a nitrosylated  $PGF_1$ , a nitrosylated  $PGF_1$ , a nitrosylated  $PGF_2$ , a nitrosylated  $PGF_{2\alpha}$ , a nitrosated and nitrosylated  $PGF_{2\alpha}$ , a nitrosated rioprostil, a nitrosylated rioprostil, a nitrosated and nitrosylated rioprostil, a nitrosated rosaprostol, a nitrosylated rosaprostol, a nitrosated and nitrosylated rosaprostol, a nitrosated remiprostol, a nitrosylated remiprostol, a nitrosated and nitrosylated remiprostol, a nitrosated sulprostone, a nitrosylated sulprostone, a nitrosated and nitrosylated sulprostone, a nitrosated trimoprostil, a nitrosylated trimoprostil, a nitrosated and nitrosylated trimoprostil, a nitrosated tiprostanide, a nitrosylated tiprostanide, a

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 6 of 14

nitrosated and nitrosylated tiprostanide, a nitrosated unoprostone, a nitrosylated unoprostone, a nitrosated and nitrosylated unoprostone, a nitrosated viprostol, a nitrosylated viprostol, a nitrosylated viprostol or a mixture thereof.

- 4. (Original) A composition comprising the compound of claim 2 and a pharmaceutically acceptable carrier.
- 5. (Original) A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 4.
  - 6. (Original) The method of claim 5, wherein the patient is female.
  - 7. (Original) The method of claim 5, wherein the patient is male.
- 8. (Original) The method of claim 5, wherein the composition is administered orally, by intracavernosal injection, by transurethral application, or by transdermal application.
  - 9. (Cancelled)
- 10. (Original) The composition of claim 4, further comprising at least one vasoactive agent or a pharmaceutically acceptable salt thereof.
- 11. (Original) The composition of claim 10, wherein the vasoactive agent is a potassium channel activator, a calcium channel blocker, an  $\alpha$ -blocker, a  $\beta$ -blocker, a phosphodiesterase inhibitor, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, an endothelin antagonist or a mixture thereof.
- 12. (Original) The composition of claim 10, wherein the vasoactive agent is an  $\alpha$ -blocker or a phosphodiesterase inhibitor.
- 13. (Original) The composition of claim 12, wherein the  $\alpha$ -blocker is phentolamine, prazosin, doxazosin, terazosin, yohimbine or moxisylyte and the phosphodiesterase inhibitor is papaverine, zaprinast, sildenafil or IC 351, or a mixture thereof.
- 14. (Original) A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 10.
  - 15. (Original) The method of claim 14, wherein the patient is female.
  - 16. (Original) The method of claim 14, wherein the patient is male.

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 7 of 14

- 17. (Original) The method of claim 14, wherein the composition is administered orally, by intracavernosal injection, by transurethral application or by transdermal application.
  - 18. (Canceled)
- 19. (Previously Presented) A composition comprising at least one compound of claim 2 or a pharmaceutically acceptable salt thereof, and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.
- 20. (Previously Presented) The composition of claim 19, further comprising a pharmaceutically acceptable carrier.
- 21. (Original) The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor or is a substrate for nitric oxide synthase is an S-nitrosothiol.
- 22. (Original) The composition of claim 21, wherein the S-nitrosothiol is S-nitroso-N-acetylcysteine, S-nitroso-captopril, S-nitroso-N-acetylpenicillamine, S-nitroso-homocysteine, S-nitroso-cysteine or S-nitroso-glutathione.
  - 23. (Original) The composition of claim 21, wherein the S-nitrosothiol is:
  - (i)  $HS(C(R_e)(R_f))_mSNO;$
  - (ii)  $ONS(C(R_e)(R_f))_mR_e$ ; and
  - $(iii) \qquad H_2N\text{-}CH(CO_2H)\text{-}(CH_2)_m\text{-}C(O)NH\text{-}CH(CH_2SNO)\text{-}C(O)NH\text{-}CH_2\text{-}CO_2H; \\$

wherein m is an integer from 2 to 20;  $R_e$  and  $R_f$  are each independently a hydrogen, an alkyl, a cycloalkoxy, a halogen, a hydroxy, an hydroxyalkyl, an alkoxyalkyl, an arylheterocyclic ring, an alkylaryl, a cycloalkylalkyl, a heterocyclicalkyl, an alkoxy, a haloalkoxy, an amino, an alkylamino, a dialkylamino, an arylamino, a diarylamino, an alkylarylamino, an alkoxyhaloalkyl, a haloalkoxy, a sulfonic acid, a sulfonic ester, an alkylsulfonic acid, an arylsulfonic acid, an arylalkoxy, an alkylthio, an arylthio, a cycloalkylthio, a cycloalkenyl, a cyano, an aminoalkyl, an aminoaryl, an aryl, an arylalkyl, an alkylaryl, a carboxamido, a alkylcarboxamido, an arylcarboxamido, an amidyl, a carboxyl, a carbamoyl, a carbamate, an alkylcarboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, a haloalkoxy, a sulfonamido, an alkylsulfonamido, an arylsulfonamido, a sulfonic ester, a urea, a phosphoryl, a nitro, -T-Q, or  $(C(R_e)(R_f))_k$ -T-Q, or

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 8 of 14

 $R_e$  and  $R_f$  taken together with the carbons to which they are attached form a carbonyl, a methanthial, a heterocyclic ring, a cycloalkyl group or a bridged cycloalkyl group; Q is -NO or -NO<sub>2</sub>; and T is independently a covalent bond, a carbonyl, an oxygen, -S(O)<sub>0</sub>- or -N(R<sub>a</sub>)R<sub>i</sub>-, wherein o is an integer from 0 to 2, R<sub>a</sub> is a lone pair of electrons, a hydrogen or an alkyl group;  $R_i$  is a hydrogen, an alkyl, an aryl, an alkylcarboxylic acid, an aryl carboxylic acid, an alkylcarboxylic ester, an arylcarboxylic ester, an alkylcarboxamido, an arylcarboxamido, an alkylsulfinyl, an alkylsulfonyl, an arylsulfinyl, an arylsulfonyl, a sulfonamido, a carboxamido, a carboxylic ester, an amino alkyl, an amino aryl, -CH<sub>2</sub>-C(T-Q)(R<sub>e</sub>)(R<sub>f</sub>), or -(N<sub>2</sub>O<sub>2</sub>-)·M<sup>+</sup>, wherein M<sup>+</sup> is an organic or inorganic cation; with the proviso that when R<sub>i</sub> is -CH<sub>2</sub>-C(T-Q)(R<sub>e</sub>)(R<sub>f</sub>) or -(N<sub>2</sub>O<sub>2</sub>-)·M<sup>+</sup>; then "-T-Q" can be a hydrogen, an alkyl group, an alkoxyalkyl group, an aminoalkyl group, a hydroxy group or an aryl group.

- 24. (Original) The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase, is L-arginine, L-homoarginine, N-hydroxy-L-arginine, nitrosated L-arginine, nitrosylated L-arginine, nitrosylated L-arginine, nitrosylated N-hydroxy-L-arginine, citrulline, ornithine, glutamine, lysine, polypeptides comprising at least one of these amino acids or inhibitors of the enzyme arginase.
- 25. (Previously Presented) The composition of claim 19, wherein the compound that donates, transfers, or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase is:
  - (i) a compound that comprises at least one ON-O-, ON-N- or ON-C- group;
- (ii) a compound that comprises at least one  $O_2N$ -O-,  $O_2N$ -N-,  $O_2N$ -S- or - $O_2N$ -C- group;
- (iii) a N-oxo-N-nitrosoamine having the formula: R<sup>1</sup>R<sup>2</sup>-N-N(O-M<sup>+</sup>)-NO, wherein R<sup>1</sup> and R<sup>2</sup> are each independently a polypeptide, an amino acid, a sugar, an oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted hydrocarbon, or a heterocyclic group, and M<sup>+</sup> is an organic or inorganic cation.
- 26. (Original) The composition of claim 25, wherein the compound comprising at least one ON-O-, ON-N- or ON-C- group is an ON-O-polypeptide, an ON-N-polypeptide, an

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 9 of 14

ON-C-polypeptide, an ON-O-amino acid, an ON-N-amino acid, an ON-C-amino acid, an ON-O-sugar, an ON-N-sugar, an ON-C-sugar, an ON-O-oligonucleotide, an ON-N-oligonucleotide, an ON-C-oligonucleotide, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-O-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-N-hydrocarbon, a straight or branched, saturated or unsaturated, substituted or unsubstituted, aliphatic or aromatic ON-C-hydrocarbon, an ON-O-heterocyclic compound, an ON-N-heterocyclic compound or a ON-C-heterocyclic compound.

- 27. (Original) The composition of claim 25, wherein compound comprising at least one O<sub>2</sub>N-O-, O<sub>2</sub>N-N-, O<sub>2</sub>N-S- or O<sub>2</sub>N-C- group is an O<sub>2</sub>N-O-polypeptide, an O<sub>2</sub>N-N-polypeptide, an O<sub>2</sub>N-S-polypeptide, an O<sub>2</sub>N-C-polypeptide, an O<sub>2</sub>N-O-amino acid, O<sub>2</sub>N-N-amino acid, O<sub>2</sub>N-S-amino acid, an O<sub>2</sub>N-C-amino acid, an O<sub>2</sub>N-O-sugar, an O<sub>2</sub>N-N-sugar, O<sub>2</sub>N-S-sugar, an O<sub>2</sub>N-C-sugar, an O<sub>2</sub>N-O-oligonucleotide, an O<sub>2</sub>N-N-oligonucleotide, an O<sub>2</sub>N-S-oligonucleotide, an O<sub>2</sub>N-C-oligonucleotide, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O<sub>2</sub>N-O-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted O<sub>2</sub>N-N-hydrocarbon, a straight or branched, saturated or unsaturated, aliphatic or aromatic, substituted or unsubstituted or unsubst
- 28. (Original) A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 19.
  - 29. (Original) The method of claim 28, wherein the patient is female.
  - 30. (Original) The method of claim 28, wherein the patient is male.
- 31. (Original) The method of claim 28, wherein the composition is administered orally, by intracavernosal injection, by transurethral application or by transdermal application.
  - 32. (Canceled)
- 33. (Original) The composition of claim 19, further comprising at least one vasoactive agent or a pharmaceutically acceptable salt thereof.

Response and Amendment under 37 CFR § 1.111 Application No. 09/516,194 Page 10 of 14

- 34. (Original) The composition of claim 33, wherein the vasoactive agent is a potassium channel activator, a calcium channel blocker, an  $\alpha$ -blocker, a  $\beta$ -blocker, a phosphodiesterase inhibitor, adenosine, an ergot alkaloid, a vasoactive intestinal peptide, a dopamine agonist, an opioid antagonist, an endothelin antagonist or a mixture thereof.
- 35. (Original) The composition of claim 34, wherein the vasoactive agent is an  $\alpha$ -blocker or a phosphodiesterase inhibitor.
- 36. (Original) The composition of claim 35, wherein the  $\alpha$ -blocker is phentolamine, prazosin, doxazosin, terazosin, yohimbine or moxisylyte and the phosphodiesterase inhibitor is papaverine, zaprinast, sildenafil or IC 351, or a mixture thereof.
- 37. (Original) A method for treating a sexual dysfunction in a patient in need thereof comprising administering to the patient a therapeutically effective amount of the composition of claim 33.
  - 38. (Original) The method of claim 37, wherein the patient is female.
  - 39. (Original) The method of claim 37, wherein the patient is male.
- 40. (Original) The method of claim 37, wherein the composition is administered orally, by intracavernosal injection, by transurethral application or by transdermal application.

Claims 41-103 (Cancelled)

- 104. (Original) A kit comprising at least one compound of claim 2 and at least one compound that donates, transfers or releases nitric oxide, or induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase.
- 105. (Original) The kit of claim 104, wherein the compound of claim 2 and the at least one compound that donates, transfers or releases nitric oxide, induces the production of endogenous nitric oxide or endothelium-derived relaxing factor, or is a substrate for nitric oxide synthase are separate components in the kit or are in the form of a composition in the kit.
  - 106. (Original) The kit of claim 104, further comprising at least one vasoactive agent. 107-115. (Canceled)
- 116. (New) A prostaglandin comprising at least one NO group or a pharmaceutically acceptable salt thereof; wherein the at least one NO group is linked to the prostaglandin compound through an oxygen atom, a nitrogen atom or a sulfur atom.